PATENT
Client/Matter No. 18950-68

I hereby certify that on October 12, 2001, this document (along with any paper referred to as being attached or enclosed) is being deposited with the United States Postal Service, Express mail, in an envelope addressed to the Assistant Commissioner for Patents, Box Patent Application Washington, D.C. 20231 **Express Mail No. EL585705510US**

Florence Thys-Doucet

Applicant: Jorma Virtanen
Serial No.: To Be Assigned
Filed: October 12, 2001
Title: Assay Device and Method
Examiner: Unknown
Group Art Unit: Unknown

Parent App. Serial No. 09/632,113
Filed: August 3, 2000

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Attn: Box Non-Fee Amendment
Assistant Commissioner for Patents
Washington, D.C. 20231

PRELIMINARY AMENDMENT

Sir:

Please enter the following Preliminary Amendment:

IN THE TITLE

Please amend the title to read -- ASSAY DEVICE AND METHOD --

IN THE SPECIFICATION

Please amend the specification as follows a marked up copy is appended hereto to show changes:

On page 13, line 16, change "5A" to -- 5 -- .

Figure 5 is a schematic representation of the chemical structure of an exemplary cleavable spacer molecule of the cleavable reflective signal element of this invention, subsequent to its attachment to the derivatized plastic substrate surface of the assay device but prior to derivatization with oligonucleotide side members, in which piv denotes a pivaloyl protective group, MMT denotes monomethoxytrityl, and n and m each independently represents an integer greater than or equal to one;

On page 69, delete lines 28-31 and insert:

--	Ia:	5'-CGGGTGTGG (SEQ. ID. NO. 1)	Ib:	CGGCCGCGG-3' (SEQ. ID. NO. 5)
	IIa:	5'-CGGGTGTGA (SEQ. ID. NO. 2)	IIb:	CGGCCGCGG-3' (SEQ. ID. NO. 5)
	IIIa:	5'-CGGGTGTGC (SEQ. ID. NO. 3)	IIIb:	CGGCCGCGG-3' (SEQ. ID. NO. 5)

IVa: 5‘-CGGGTGTGT (SEQ. ID. NO. 4) IVb: CGGCCGCGG-3‘ (SEQ. ID. NO. 5) --

On page 70, line 11 after “5‘-GCCCACACCGCCGGCGCC-3‘”, insert -- (SEQ. ID. NO. 6) --;

A test sample containing 5’ -GCCCACACCGCCGGCGCC-3 (SEQ. ID. NO. 6) is prepared and allowed to contact the cleavable signal element at a temperature that approximates the T_m of the side members Ia and Ib. The temperature of the sample solution is heated to about 20 degrees Centigrade above the T_m. Subsequently, the signal element is treated with 0.1M sodium fluoride solution and washed. Spacer molecules remaining attached to the surface signal the presence of, and tethering by, 5’ -GCCCACACCGCCGGCGCC-3’ (SEQ. ID. NO. 6).

line 19, after “5‘-GCCCACACCGCCGGCGCC-3‘”, insert -- (SEQ. ID. NO. 6) --;

A test sample containing 5’ -GCCCACACCGCCGGCGCC-3 (SEQ. ID. NO. 6) is prepared and allowed to contact the cleavable signal element at a temperature that approximates the T_m of the side members Ia and Ib. The temperature of the sample solution is heated to about 20 degrees Centigrade above the T_m. Subsequently, the signal element is treated with 0.1M sodium fluoride solution and washed. Spacer molecules remaining attached to the surface signal the presence of, and tethering by, 5’ -GCCCACACCGCCGGCGCC-3’ (SEQ. ID. NO. 6).

line 21, after “5‘GCCCACACTGCCGGCGCC-3‘”, insert -- (SEQ. ID. NO. 7) --;

line 21, delete “5-GCCCACACGGCCGGCGCC-3‘”, and insert -- 5‘-GCCCACACGGCCGGCGCC-3‘ (SEQ. ID. NO. 8) --; and

line 22, after “5‘-GCCCACAGCCGGCGCC-3‘”, insert -- (SEQ. ID. NO. 9) --.

On page 71, line 14, after “TGT-3‘” insert -- (SEQ. ID. NO. 10); and

Primer 1: 5’ -TGA GAC ACC AGG AAT TAG ATA TCA GTA CAA TGT-3’ (SEQ. ID. NO. 10)

On page 71, line 15, after “TGT-3‘”, insert -- (SEQ. ID. NO. 11) --.

Primer 2: 5' -CTA AAT CAG ATC CTA CAT ATA AGT CAT CCA TGT-3' (SEQ. ID. NO. 11)

On page 72, line 1, after "CAA-3'", insert -- (SEQ. ID. NO. 12) --; and

Cleavable spacers with siloxane moiety are synthesized and attached in a uniform density to a derivatized 120 mm polycarbonate disk substrate essentially as set forth in sections 5.2 and 5.3 hereinabove. The following side members are then stamped on the cleavable spacers:

first side member: 5' -TAG ATA TCA GTA CAA-3' (SEQ. ID. NO. 12)

line 2, after "ACA-5'", insert -- (SEQ. ID. NO. 13).

second side member: 3' -TAT TCA GTA GGT ACA-5' (SEQ. ID. NO. 13)

After page 72, please add the attached SEQUENCE LISTING (new pages 73-76).

IN THE ABSTRACT

Please delete the present abstract as follows:

[A cleavable signal element for use in quantitative and qualitative assay devices and methods is described. Binding of the chosen analyte simultaneously to a first and second analyte-specific side member of the cleavable signal element tethers the signal-responsive moiety to the signal element's substrate-attaching end, despite subsequent cleavage at the cleavage site that lies intermediate the first and second side members. Assay devices comprising the cleavable signal elements are described, as are analytic methods adapted to their use. The analytic devices of the present invention may be adapted to detection using conventional CD-ROM or DVD readers.]

and substitute therefor the following new Abstract:

-- An assay device and method includes assay sectors provided within a software encoded laser detector readable disc. A sample inlet port is associated with each of the sectors which include analyte binding elements segregated within the disc. The computer software is encoded in an area of a substrate of the disc which is spatially distinct from the assay sectors for independent reading of the elements relative the software by the same laser and laser disc reader. The exemplary analyte binding

elements include cleavable signal elements provided in a spatially addressable pattern with cleavable spacers and a signal responsive moiety adapted to reflect or scatter incident light. --

IN THE CLAIMS:

Please cancel Claim 1.

Please add the following new claims:

53. An assay device comprising:

a laser readable disk;

one or more individual assay sectors including analyte binding elements within said disk to be scanned by the incident beam of a laser of a laser disc reader;

a sample inlet port associated with each of said one or more assay sectors to be scanned by the incident beam of, and read by, a laser disk reader;

computer software encoded in said disk which is encoded in an area of said disk which is spatially separate from said assay sectors to allow separate scanning of said software and said sectors; and

said sectors and software being provided in said disk for being read by the same laser disk reader.

54. The assay device of claim 53 wherein said elements are provided within said sectors within said disk in a predetermined spatially addressable manner.

55. The assay device of any one of claims 53 and 54 wherein said software includes information selected from the group: tracking information for tracking of an incident laser, assay interpretive algorithms, standard control values and self-diagnostics.

56. The assay device of claim 55 wherein said software is capable of uploading diagnostic information to remote locations.

57. The assay device of any one of claims 53 and 54 wherein said analyte binding elements include cleavable signal elements having a cleavable spacer and a signal responsive moiety.

58. The assay device of claim 57 wherein said signal responsive moiety is adapted to reflect or scatter incident light.

59. The assay device according to claim 57, wherein said signal responsive moiety is a metal microsphere.

60. The assay device according to claim 59, wherein said metal microsphere is essentially a metal selected from the group of gold, silver, nickel, platinum, chromium and copper.

61. The assay device according to claim 59, wherein said metal is essentially gold.

62. The assay device according to claim 59, wherein said metal microsphere is ferromagnetic.

63. The assay device according to claim 57, wherein said cleavable spacer includes a first side member and a second side member, said members including oligonucleotides.

64. The assay device according to claim 63, wherein said first and second side member oligonucleotides are 5mers - 20mers.

65. The assay device according to claim 57, wherein said cleavable spacer includes a first side member having a first antibody, and a second side member having a second antibody.

66. A laser light detector readable disk comprising:

signal elements in a spatially addressable pattern;

interpretive software encoded in an area of said disk which is spatially distinct from and laterally spaced on said disk from said elements; and

said elements and software are readable by a same disk reader.

67. The disk of claim 66 wherein said software is encoded in the form of a spiral track located in a central area of said disk.

68. The disk of any one of claims 66 and 67 wherein the disposition of said signal elements in said pattern is suitable for the assay of multiple samples in parallel.

69. The disk of claim 68 wherein a substrate of said disk is provided with one or more microfabricated chambers to receive and segregate individual assay sectors of said elements.

70. The disk of claim 69 wherein a sample inlet port is provided for each of said one or more chambers.

71. The disk of claim 66 wherein said software includes information for controlling the tracking of an incident laser.

72. The disk of claim 66 wherein said software includes assay interpretive algorithms.

73. The disk of claim 66 wherein said software includes information for standard control values.

74. The disk of claim 66 wherein said signal elements are capable of reflecting or scattering incident laser light.

75. The disk of claim 66 wherein said software is encoded in a semi-reflective layer.

76. The disk of claim 75 wherein said semi-reflective layer is formed from a metal.

77. The disk of claim 66 wherein said disk is provided with an address line to which the deposition of said signal elements is addressable.

78. The disk of claim 77 wherein the disposition of said signal elements is on annular tracks.

79. The disk of claim 77 wherein the disposition of said signal elements is of a spiral configuration.

80. A laser light detector readable disk comprising:

one or more assay sectors individually segregated within said disk for individual detector inspection of a sample introduced into a respective sector by laser light;

a sample inlet port associated with each of said one or more assay sectors; and

laser light detectable software encoded in said disk in an area spatially distinct in a lateral direction of the disk from said assay sectors.

81. The disk of claim 80 wherein said software is separately readable from said one or more assay sectors.

82. The disk of claim 80 wherein analyte binding elements are provided within at least one of said one or more of said sectors.

83. The disk of claim 82 wherein said analyte binding elements include cleavable signal elements having a cleavable spacer and a signal responsive moiety.

84. The disk of claim 83 wherein said signal responsive moiety is adapted to reflect or scatter incident light.

85. The disk of claim 82 wherein said cleavable spacer includes a first side member and a second side member, said members including oligonucleotides.

86. The disk of claim 81 wherein said analyte binding elements include oligonucleotides to bind an analyte within said sector for inspection by a laser light detector.

87. The disk of claim 81 further comprising address information encoded in said disk spatially adjacent said one or more assay sectors to provide location information as to said one or more assay sectors.

88. The disk of claim 87 wherein a plurality of said sectors are positioned about said disk in spaced relation and said address information is encoded in said disk between said sectors.

89. A method for conducting an inspection of an analyte preselected for detection through the use of a laser disk and laser disk reader having an incident laser which scans the disk under the control of an associated computer, comprising:

providing one or more analyte binding elements in a predetermined first location on or within a substrate of a laser readable disk,

introducing a sample, suspected of including an analyte which will bind to said one or more elements, to said predetermined first location,

reading software information, including incident laser tracking control information, encoded on or in said disk in a second location which is spaced separate and laterally relative said disc from said first location; and

scanning said incident laser under the control of a computer over said predetermined location to determine a presence or absence of an analyte at said location using said tracking control information.

90. The method of claim 89 wherein a plurality of analyte binding elements are provided in a spatially addressable pattern.

91. The method of claim 90 wherein address information is encoded in said disc which is used in the scanning of said incident laser to address a location to be scanned.

REMARKS

It is requested that this Preliminary Amendment be entered before the examination of the within application.

Any additional fees which are required in connection with this communication and which are not specifically provided for herewith are authorized to be charged to deposit account no. 16-2230. Any overpayments are also authorized to be credited to this account.

Respectfully submitted,

October 12, 2001

Guy Porter Smith, Reg. No. 20,142
Attorney for Applicant

OPPENHEIMER WOLFF & DONNELLY LLP
2029 Century Park East, 38th Floor
Los Angeles, CA 90067-3024
Telephone: (310) 788-5000 • Fax: (310) 788-5100

Marked Up Copy of Specification to Show Changes

Figure [5A] 5 is a schematic representation of the chemical structure of an exemplary cleavable spacer molecule of the cleavable reflective signal element of this invention, subsequent to its attachment to the derivatized plastic substrate surface of the assay device but prior to derivatization with oligonucleotide side members, in which piv denotes a pivaloyl protective group, MMT denotes monomethoxytrityl, and n and m each independently represents an integer greater than or equal to one;

[Ia: 5' -CGGGTGTGG Ib: CGGCCGCGG-3'

IIa: 5' -CGGGTGTGA IIb: CGGCCGCGG-3'

IIIa: 5' -CGGGTGTGC IIIb: CGGCCGCGG-3'

IVa: 5' -CGGGTGTGT IVb: CGGCCGCGG-3']

Ia: 5' -CGGGTGTGG (SEQ. ID. NO. 1) Ib: CGGCCGCGG-3' (SEQ. ID. NO. 5)

IIa: 5' -CGGGTGTGA (SEQ. ID. NO. 2) IIb: CGGCCGCGG-3' (SEQ. ID. NO. 5)

IIIa: 5' -CGGGTGTGC (SEQ. ID. NO. 3) IIIb: CGGCCGCGG-3' (SEQ. ID. NO. 5)

IVa: 5' -CGGGTGTGT (SEQ. ID. NO. 4) IVb: CGGCCGCGG-3' (SEQ. ID. NO. 5)

A test sample containing 5' -GCCCACACCGCCGGCGCC-3 (SEQ. ID. NO. 6) is prepared and allowed to contact the cleavable signal element at a temperature that approximates the T_m of the side members Ia and Ib. The temperature of the sample solution is heated to about 20 degrees Centigrade above the T_m. Subsequently, the signal element is treated with 0.1M sodium fluoride solution and washed. Spacer molecules remaining attached to the surface signal the presence of, and tethering by, 5' -GCCCACACCGCCGGCGCC-3' (SEQ. ID. NO. 6).

The foregoing process is applied to the analysis of 5'GCCCACACTGCCGGCGCC-3' (SEQ. ID. NO. 7), [5-GCCCACACGGCCGGCGCC-3'] 5'-GCCCACACGGCCGGCGCC-3' (SEQ. ID. NO. 8) and 5' -GCCCACAGCCGGCGCC-3' (SEQ. ID. NO. 9), using, respectively, spacer molecules incorporating side members IIa and IIb, IIIa and IIIb, and IVa and IVb.

Primer 1: 5' -TGA GAC ACC AGG AAT TAG ATA TCA GTA CAA TGT-3' (SEQ. ID. NO. 10)

Primer 2: 5' -CTA AAT CAG ATC CTA CAT ATA AGT CAT CCA TGT-3' (SEQ. ID. NO. 11)

Cleavable spacers with siloxane moiety are synthesized and attached in a uniform density to a derivatized 120 mm polycarbonate disk substrate essentially as set forth in sections 5.2 and 5.3 hereinabove. The following side members are then stamped on the cleavable spacers:

first side member: 5' -TAG ATA TCA GTA CAA-3' (SEQ. ID. NO. 12)

second side member: 3' -TAT TCA GTA GGT ACA-5' (SEQ. ID. NO. 13)